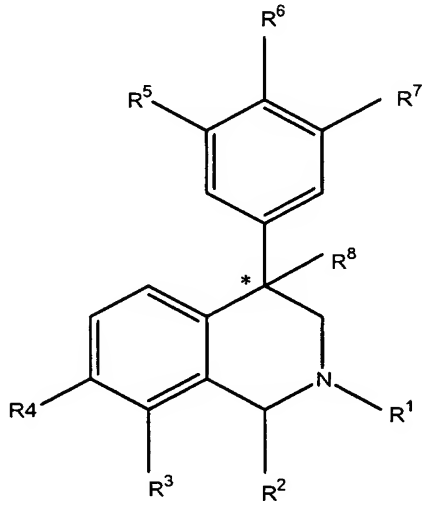
CLAIMS:

What is claimed is:

1. A method of treating chronic or neuropathic pain, treating or preventing migraine headaches, or treating stress, urge or mixed urinary incontinence comprising administering to a patient in need thereof an effective amount of a compound of the formula (1):



(1)

wherein:

the carbon atom designated * is in the R or S configuration;

R^1 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, each of which is optionally substituted with from 1 to 3 substituents independently selected at each occurrence thereof from C_1-C_3 alkyl, halogen, Ar, -CN, $-OR^9$ and $-NR^9R^{10}$;

R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_4- C_7 cycloalkylalkyl or C_1-C_6 haloalkyl;

R^3 is H, halogen, $-OR^{11}$, $-S(O)_nR^{12}$, -CN, $-C(O)R^{12}$, $-C(O)NR^{11}R^{12}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl and wherein each of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_4-C_7 is optionally substituted with from 1 to 3 substituents independently selected at each occurrence thereof from C_1-C_3 alkyl, halogen, -CN, $-OR^9$, $-NR^9R^{10}$ and phenyl which is optionally substituted 1-3 times with halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy, - CN, $-OR^9$, or $-NR^9R^{10}$;

R^4 is aryl selected from phenyl, naphthyl and indenyl, or heteroaryl selected from pyridyl, pyrimidinyl, triazinyl, triazolyl, furanyl, pyranyl, indazolyl, benzimidazolyl, quinolinyl, quinazolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, benzthiazolyl, purinyl, isothiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, oxadiazolyl and thiadiazolyl, wherein the aryl or heteroaryl group is optionally substituted with from 1 to 4 R^{14} substituents;

R^5 and R^6 and R^7 are each independently H or are selected from halogen, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{12}$, $-NR^{11}C(O)_2R^{12}$, $-NR^{11}C(O)NR^{12}R^{13}$, $-S(O)_nR^{12}$, -CN, $-C(O)R^{12}$, $-C(O)NR^{11}R^{12}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl or C_4-C_7 cycloalkylalkyl, and wherein each of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl and C_4-C_7 cycloalkylalkyl is optionally substituted with from 1 to 3 substituents independently selected at each occurrence thereof from C_1-C_3 alkyl, halogen, -CN, $-OR^9$, $-NR^9R^{10}$ and phenyl which is optionally substituted 1-3 times with halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy, -CN, $-OR^9$, or $-NR^9R^{10}$; or R^5 and R^6 may be -0- $C(R^{12})_2$-0-;

R^8 is H, halogen or OR^{11};

R^9 and R^{10} are each independently H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, $-C(O)R^{13}$, phenyl or benzyl, where phenyl or benzyl is optionally substituted from 1 to 3 times with a substituent selected independently at each occurrence thereof from halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 alkoxy;

or R^9 and R^{10} are taken together with the nitrogen to which they are attached to form a piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine ring;

R^{11} is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, $-C(O)R^{13}$, phenyl or benzyl, where phenyl or benzyl is optionally substituted 1 to 3 times with halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy;

R^{12} is H, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl, phenyl or benzyl, where phenyl or benzyl is optionally substituted 1 to 3 times with halogen, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 alkoxy;

or R^{11} and R^{12} are taken together with the nitrogen to which they are attached to form a piperidine, pyrrolidine, piperazine, N- methylpiperazine, morpholine or thiomorpholine ring, with the proviso that only one of R^9 and R^{10} or R^{11} and R^{12} are taken together with the nitrogen to which they are attached to form a piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine ring;

R^{13} is C_1-C_4 alkyl, C_1-C_4 haloalkyl or phenyl;

n is 0, 1, or 2; and,

R^{14} is independently selected at each occurrence from a substituent selected from the group: halogen, $-NO_2$, $-OR^{11}$, $-NR^{11}R^{12}$, $-NR^{11}C(O)R^{12}$, $-NR^{11}C(O)_2R^{12}$, $-NR^{11}C(O)NR^{12}R^{13}$, $-S(O)_nR^{12}$, -CN, $-C(O)R^{12}$, $-C(O)NR^{11}R^{12}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, and C_4-C_7 cycloalkylalkyl where C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_4-C_7 cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from the group consisting of C_1- C_3 alkyl, halogen, Ar, -CN, $-OR^9$, and $-NR^9R^{10}$, or

an oxide thereof, a pharmaceutically acceptable salt thereof, a solvate thereof, or prodrug thereof.

2. A method of claim 1, wherein R^1 is C_1-C_6 alkyl.

3. A method of claim 2, wherein R^1 is methyl.

4. A method of claim 1, wherein R^2 is H, C_1-C_6 alkyl or C_1-C_6 haloalkyl.

5. The compound of claim 4, wherein R^2 is H or C_1-C_6 alkyl.

6. A method of claim 5, wherein R^2 is H.

7. A method of claim 1, wherein R^3 is H, halogen, $-OR^{11}$, $-S(O)_2R^{12}$, C_1-C_6 alkyl or substituted C_1-C_6 alkyl.

8. A method of claim 7, wherein R^3 is H.

9. A method of claim 1, wherein R^4 is phenyl optionally and independently substituted from 1 to 4 times with R^{14}.

10. A method of claim 9, wherein the R^4 is phenyl, 2-chlorophenyl, 3-chlorophenyl, 4 chlorophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl or 4 dimethylaminophenyl.

11. A method of claim 1, wherein R^4 is pyridyl, pynmidinyl, triazinyl, triazolyl, furanyl, pyranyl, indazolyl, benzimidazolyl, quinolinyl, quinazolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, benzthiazolyl, puninyl, isothiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, oxadiazolyl, or thiadiazolyl, which is optionally substituted 1-4 times with R^{14}.

12. A method of claim 11, wherein R^4 is 4-methyl-2-furanyl, 5-methyl- 2-furanyl, 3-furanyl, 2-thienyl, 3-thienyl, 3,5-dimethyl-4-isoxazolyl, 2- pyridyl, 3-pyridyl, 4-pyridyl, 2-methoxy-3-pyridyl, 6-methoxy-3pyridyl, 3, 5-pyrimidinyl or 2,6-pyrimidinyl.

13. The compound of claim 1, wherein R^5, R^6 and R^7 are each independently selected from the group: H, halogen, $-OR^{11}$, $-NR^{11}R^{12}$, -, $-S(O)_2R^{12}$, $-C(O)R^{12}$, and optionally substituted C_1-C_6 alkyl.

14. A method of claim 13, wherein R^7 is H.

15. A method of claim 14, wherein of R^5 and R^6 are each H, F, Cl, OH, OCH_3 or CH_3- .

16. A method of claim 1, wherein R^8 is H, OH, or F.

17. A method of claim 1, wherein

R^1 is C_1-C_6 alkyl;

R^2 is H, C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^3 is H, halogen, $-OR^{11}$, $-S(O)_2R^{12}$, C_1-C_6 alkyl or substituted C_1-C_6 alkyl;

R^4 is aryl or heteroaryl; and

R^5, R^6 and R^7 are each independently selected from the group: H, halogen, -OR^{11}, $NR^{11}R^{12}$, -$S(O)_2R^{12}$, -$C(O)R^{12}$, C_1-C_6 alkyl and substituted C_1-C_6 alkyl.

18. A method of claim 1, wherein R^1 is methyl;

R^2 is H;

R^3 is H;

R^5 and R^6 are each independently selected from the group: H, F, Cl, OH, OCH_3, and CH_3;

R^7 is H or F;

R^8 is H, OH, or F; and

R^4 is phenyl, pyridyl, pyrimidinyl, triazinyl, triazolyl, furanyl, pyranyl, indazolyl, thienyl, imidazolyl, thiazolyl, purinyl, isothiazolyl, indolyl, pyrrolyl, oxazolyl, isoxazolyl, or pyrazolyl, each of which R^4 is optionally and independently substituted from 1-4 times with R^{14}.

19. A method of claim 1, wherein R^1 is methyl;

R^2 is H;

R^3 is H;

R^5 and R^6 are each H, F or CH_3;

R^7 is H;

R^8 is H; and

R^4 is phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-methoxyphenyl, 3 methoxyphenyl, 4-methoxyphenyl, 4-dimethylaminophenyl, 4-methyl-2-furanyl, 5 methyl-2-furanyl and 3-furanyl, 2-thienyl and 3-thienyl, 3,5-dimethyl-4- isoxazolyl, 2 pyridyl, 3-pyridyl, 4-pyridyl, 2-methoxy-3-pyridyl and 6-methoxy-3-pyridyl 3,5 pyrimidinyl or 2,6-pyrimidinyl.

20. A method according to claim 1, wherein the carbon atom designated * is in the R configuration.

21. A method according to claim 1, wherein the carbon atom designated * is in the S configuration.

22. A method comprising a mixture of stereoisomerisms compounds of claim 1 wherein the carbon atom designated * is in the S or R configuration.

23. A method according to claim 1, selected from the group:

4,7-diphenyl-2-methyl- 1,2,3,4-tetrahydroisoquinoline;

7-(2-chloro)phenyl-2-methyl-4-phenyl- 1,2,3,4-tetrahydroisoquinoline;

7-(3-chloro)phenyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(4-chloro)phenyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(2-methoxy)pheny1-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(3-methoxy)phenyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(4-methoxy)phenyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(4-N,N-dimethylamino)phenyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7- [(4-methyl)-2-thienyl -2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-[(5-methyl)-2-furanyl]-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

7-(3-furanyl)-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(2-thienyl)-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(3-thienyl)-1,2,3,4-tetrahydroisoquinoline;

7- [(3,5-dimethyl)-4-isoxazole]-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(2-pyridyl)-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(3-pyridyl)-1,2,3,4-tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(4-pyridyl)-1,2,3,4-tetrahydroisoquinoline;

4-(3,4-difluoro)phenyl-2-methyl-7-(3-pyridyl)-1,2,3,4- tetrahydroisoquinoline;

7-[(2-methoxy)-3-pyridyll-2-methyl-4-phenyl-1,2,3,4- tetrahydroisoquinoline;

7-[(6-methoxy)-3-pyridyll-2-methyl-4-phenyl-1,2,3,4- tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(3,5-pyrimidyl)-1,2,3,4-tetrahydrolsoquinoline;

4-(3,4-difluoro)phenyl-2-methyl-7-(3,5-pyrimidyl)-1,2,3,4-tetrahydrolsoquinoline;

4-(4-methyl)phenyl-2-methyl-7-(3,5-pyrimidyl)-1,2,3,4- tetrahydroisoquinoline;

2-methyl-4-phenyl-7-(2,6-pyrimidyl)-1,2,3,4-tetrahydroisoquinoline;

7-(2,5-dimethyl-4-isoxazole)-4-(4-methoxy)phenyl-2-methyl-1,2,3,4-tetrahydroisoquinoline; and

4-(4-methoxy)phenyl-2-methyl-7-(2-pyridyl)-1,2,3,4-tetrahydroisoquinoline or an oxide thereof, a pharmaceutically acceptable salt thereof, a solvate thereof, or a prodrug thereof

24. A method according to claim 24, wherein the compound is the (+) stereoisomer.

25. A method according to claim 24, wherein the compound is the (-) stereoisomer.